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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/609,383	07/01/2003	Richard J. Feldmann	3279-Z	4498

7590 09/28/2007

Law Office of Jim Zegeer
Suite 108
801 North Pitt Street
Alexandria, VA 22314

EXAMINER	
BRUSCA, JOHN S	
ART UNIT	PAPER NUMBER
1631	

MAIL DATE	DELIVERY MODE
09/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/609,383	FELDMANN, RICHARD J.	
	Examiner	Art Unit	
	John S. Brusca	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-12 is/are pending in the application.

4a) Of the above claim(s) 3-12 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1 and 2 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

DETAILED ACTION

Specification

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR §§ 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821-1.825 for the following reasons:

SEQ ID NOS have been added to the specification in response to the objection to the specification in the Office action mailed 22 March 2006, however the computer readable form filed on 07 July 2007 is defective. Please see the Notice to comply and RSL error report attached to this Office action.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

In In re Wands (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a

determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) Quantity of experimentation: The only utility asserted by the specification is to use connectron symmetries to predict control of gene expression (see for example pages 11, 15, and 16 of the specification).In order to practice the claimed invention one of skill in the art must identify and use a connectron to predict regulation of gene expression. In some embodiments changes in connectron behavior that correlate with changes in gene expression is monitored or effected. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.

b) The amount of direction or guidance presented: The claimed invention is a method of identification of sequences that have a connectron relationship and act to modulate gene expression. On page 3, the specification defines connectrons as a tetradic structure between two sequences in an RNA transcript of a genomic sequence and two sequences in double stranded genomic DNA. The specification speculates without evidence on page 7 that triple-stranded (triplex) structures will form between RNA and double stranded DNA in chromatin where connectron symmetries are identified. The specification does not provide guidance that there are any limitations on formation of triplex structures, and only implies that regions of RNA with identical sequence to one strand of a double stranded DNA sequence will form triplex structures.

The specification does not address why all RNA transcripts of genes would not form a continuous triplex structure with the gene from which it is transcribed. The specification provides guidance to identify connectron symmetries in genomic sequences. The specification does not provide detailed guidance to use identified connectron symmetries because the specification does not show whether or not connectrons form within cells or have an effect on gene expression. The specification does not provide specific guidance for monitoring or effecting changes in connectron behavior that correlate with gene expression.

c) The presence or absence of working examples: The specification provides working examples of identification of connectron symmetries by computer-mediated searching of genomic sequences. However, the specification does not provide evidence that connectron symmetries in genomic sequences result in formation of triplex RNA-DNA structures or that if connectron triplex structures do exist that connectrons control gene expression. The specification does not provide working examples of using identified connectron symmetries to predict effects on gene expression. The specification does not provide working examples of monitoring or effecting changes in connectron behavior that correlate with gene expression.

d) The nature of the invention: The nature of the invention, gene expression control, is complex.

e) The state of the prior art: One of skill in the art, after reading the specification, would not know that connectron symmetries identified by computer-mediated searches of genomic sequences would allow for prediction of gene expression of genes that have connectron symmetries. The specification does not provide experimental evidence that connectron

symmetries cause modulation of gene expression. Neither the prior art nor post-filing art shows connectrons. Mattick (published in 2001, one year after the effective instant filing date) reviews effects of RNA molecules on gene regulation. Mattick does not show connectrons as defined in the instant specification. Chan et al. reviews triplex DNA formation. Chan et al. shows in figures 1A-C that short stretches of oligonucleotides may form parallel or antiparallel triplex structures. Chan et al. shows in figures 1B that parallel triplex forming oligonucleotides form bonds between C and T residues of the oligonucleotide and G and A residues of the double stranded DNA molecule. Figure 1C shows that antiparallel triplex forming oligonucleotides form bonds between A, G, and T residues of the oligonucleotide and A, G, and A residues of the double stranded DNA. Chan et al. characterize the limited range of base pairing possibilities in triplex structures as pyrimidine binding motifs or purine binding motifs. Chan et al. describe on pages 268-273 the unpredictability and difficulty of forming desired triplex structures that are limited to the purine motif or the pyrimidine motif. Chan et al. does not show a mechanism that allows for triplex structures to form with any and all regions of identity between an RNA transcript and a region of double stranded DNA that has an identical sequence in one of the two strands of DNA, as required for connectron formation as defined in the instant specification.

f) The relative skill of those in the art: The skill of those in the art of gene expression is high.

g) The predictability of the art: The predictability of the relationship of connectron symmetries and gene expression is unknown in the prior art and is not described in the instant specification.

h) The breadth of the claims: The claims are broad in that they are drawn to identification and modulation of connectron symmetries whose relationship to gene expression is not established.

The skilled practitioner would first turn to the instant specification for guidance in using the claimed invention. However, the specification lacks any evidence that connectrons form in cells or that connectron symmetries are related to gene expression. As such, the skilled practitioner would turn to the prior art for such guidance, however the prior art does not discuss connectron symmetries. Chan et al. shows that triplex formation occurs only with oligonucleotides with a purine rich or pyrimidine rich motif, rather than with any identical sequence as suggested in the specification. Finally, said practitioner would turn to trial and error experimentation to determine a relationship between connectron symmetries and gene expression. Such amounts to undue experimentation.

Response to Arguments

4. Applicant's arguments filed 19 July 2007 have been fully considered but they are not persuasive.

The applicants state that the issues discussed in the rejection for lack of enablement under 35 U.S.C. 112, first paragraph are unrelated to the claimed subject matter, however enablement requires that one of skill in the art is enabled to use the claimed subject matter, and the rejection is maintained because the specification at the time of filing does not enable the use of the claimed subject matter. The applicants refer to the Vacatur mailed 28 September 2006 in Application No. 09/866925 in which the Board states that one of skill in the art would be enabled

to generate data of connectron symmetries from a genome sequence. However, the applicants have not provided any evidence in the specification or their arguments that the triplex structure of connectrons form or can be used to predict or control gene expression. The applicants argue that the claim limitations do not require that the results of the claimed methods be used to predict or control gene expression, but enablement of the claimed subject matter does require that there is an enabled patentable utility for the claimed subject matter. For this reason the rejection is maintained because a use for the claimed subject matter is not enabled.

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie A. Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/John S. Brusca/

Primary Examiner

Art Unit 1631

jsb

Continuation of Attachment(s) 6). Other: Notice to Comply, RSL Error Report.

NOTICE TO COMPLY WITH SEQUENCE RULES	Application No. 10/609,383	Applicant(s) FELDMANN, RICHARD J.	
	Examiner John S. Brusca	Art Unit 1631	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 CFR 1.821-1.825 for the following reasons:

☐ 1. This application clearly fails to comply with the requirements of 37 CFR 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 CFR 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 CFR 1.821(e).

☒ 4. A copy of the "Sequence Listing in computer readable form has been submitted. However the content of the computer readable form does not comply with the requirements of 37 CFR 1.822 and/or 1.823, as indicated on the attached copy of the marked up "Raw Sequence Listing".

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable. A Substitute computer readable form must be submitted as required by 37 CFR 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 CFR 1.821(e).

☐ 7. Other:

Applicant must provide:

☐ An initial or ☒ A substitute computer readable form copy of the Sequence Listing.

☐ An initial or ☐ A Substitute paper copy of the Sequence Listing as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same, and, where applicable, include no new matter, as required by 37 CFR 1.821(e), (f), or (g) or 1.825(b) or (d).

FOR QUESTIONS PLEASE CONTACT:

Rules Interpretation (703) 308-4216
CRF Submission Help (703) 308 4212
PatentIn software help (703) 308 6856

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE

SCORE

CRF Problem Report

SCORE experienced a problem when processing the following computer readable form (CRF):

Application Serial Number: 10609363
Filing Date: 7/19/07
Date Processed by SCORE: 7/25/07

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1. EFS-Bio (<http://www.uspto.gov/ebc/efs/downloads/documents.htm>, **EFS Submission User Manual** - ePAVE)
2. **U.S. Postal Service:** Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. **Hand Carry, Federal Express, United Parcel Service, or other delivery service (EFFECTIVE 01/14/05):** U.S. Patent and Trademark Office, Mail Stop Sequence, Customer Window, Randolph Building, 401 Dulany Street, Alexandria, VA 22314

Revised 01/20/06